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**Direct Cardiac Reprogramming: Progress and Promise.**

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**Public Summary:**

The human adult heart lacks a robust endogenous repair mechanism to fully restore cardiac function after insult; thus, the ability to regenerate and repair the injured myocardium remains a top priority in treating heart failure. The ability to efficiently generate a large number of functioning cardiomyocytes capable of functional integration within the injured heart has been difficult. However, the ability to directly convert fibroblasts into cardiomyocyte-like cells both in vitro and in vivo offers great promise in overcoming this problem. In this review, we describe the insights and progress that have been gained from the investigation of direct cardiac reprogramming. We focus on the use of key transcription factors and cardiogenic genes as well as on the use of other biological molecules such as small molecules, cytokines, noncoding RNAs, and epigenetic modifiers to improve the efficiency of cardiac reprogramming. Finally, we discuss the development of safer reprogramming approaches for future clinical application.

**Scientific Abstract:**

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